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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/717,224	11/19/2003	D. Navin Chandra	GEN-002	6022

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EXAMINER	
SKIBINSKY, ANNA	

ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/717,224	CHANDRA ET AL.	
	Examiner	Art Unit	
	ANNA SKIBINSKY	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *3,5, 6,14,16-18,20,24,26,27,35,37-39 and 41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,7-13,15,19,21-23,25,28-34,36,40 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

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DETAILED ACTION

Applicants' arguments, filed 2/12/2008, have been fully considered but they are not deemed persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1, 2, 4, 7-11, 13, 15, 19, 21-23, 25, 28-32, 34, 36, and 40 are under examination. Claims 1 and 22 have been amended.

Claim Election/Restriction

1. Claims 3, 5, 6, 14, 16-18, 20, 24, 26, 27, 35, 37-39 and 41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/06/2007.

Claim Rejections - 35 USC § 101

1. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter, for the reasons set forth in the previous Office Action and re-iterated below.

Claims 1, 2, 4, 7-13, 15, 19, 21-23, 25, 28-34, 36, and 40 are drawn to a process for proposing new genomic/proteomic related knowledge. The process for proposing the new knowledge according the claimed method involves the application of algorithms and computations of nodes, qualitative descriptors and simulated models and, therefore, involves the application of a judicial exception. Regarding inventions involving the application of a judicial exception, said application must be a practical application of the judicial exception that includes either a step of a physical transformation, or produces a useful, concrete, and tangible result (State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999)). In the instant claims, there is no step of physical transformation, thus the instant claims must recite a practical application; i.e. recite a useful, concrete, and tangible result. See MPEP 2106, in particular, Section IV, for an explanation of a concrete, tangible and useful result.

Claims 1, 2, 4, 7-13, 15, 19, 21-23, 25, 28-34, 36, and 40 do not recite a tangible result. A tangible result requires that the claim must set forth a practical application to produce a real-world result. Examples of a "real-world result" include a physical transformation of matter, or a step of communicating the result in a TANGIBLE format to a user; e.g. by outputting or displaying the result of the method. Applicant is reminded

that any amendment must be fully supported and enabled by the originally filed description.

As the claims do not recite a physical transformation of matter OR a concrete, tangible and useful result, they are not directed to statutory subject matter.

Response to Arguments

1. Applicant's arguments filed 2/12/2008 have been fully considered but they are not persuasive.

2. Applicants argue that instant claims 1 and 22 as amended recite comparing proposed biological models to actual measured data to determine a fitness score and as a result identifying one of the models as one for study. Applicants further argue that said process is "transformative by nature" in that it creates new biological models and validates their accuracy, and thus produces a tangible result.

3. In response, as currently claimed, the method recites providing concepts, proposing a biological model, simulating the model, assigning a fitness parameter, and selecting one of the proposed biological models. Said steps are drawn to non-statutory subject matter because they do not recite a "physical transformation" of matter or a tangible result. Examples of a tangible result include steps wherein the result is a "real world result" such as displaying or outputting the result in a user readable format. It is further noted that the transformation of data is insufficient to render a claim statutory because, unless the data is output or displayed to a user, said data would not be in the form of a tangible result.

Claim Rejections - 35 USC § 112-2nd paragraph

1. The rejection of claims 1, 2, 4, 7-13, 15, 19, 21-23, 25, 28-34, 36, and 40 rejected under 35 U.S.C. 112, second paragraph, is withdrawn in view of Applicant's arguments/amendments filed 3/12/2008.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 2, 4, 7, 9-12, 15, 19, 21-23, 25, 28, 30- 33, 36, 40 and 42 rejected under 35 U.S.C. 103(a) as being unpatentable over Jeong et al. (Nature vol. 407 (2000),

pages 651-654) in view of Park et al (PGPub 2003/0224363), for the reasons set froth in the previous Office Action and re-iterated below.

5. Jeong et al. teaches a network model for modeling metabolic pathways in a cell (Figure 1, page 652, col. 1, lines 8-19),as in the representative structure of claim 1, step (a) and case frame structure of claim 22, step (a). As in claims 1 and 22, step (a)(i), Jeong et al. teach nodes representing enzymes and substrates produced by the enzymes (Figure 1(e)) wherein in the metabolic network the biochemical pathways connecting two substrates are links (page 652, col. 2, lines 20-24) which correspond to claim 1 and 22, step (a)(ii) reciting case frames and qualitative descriptors representing interrelationships between two nodes and claims 7 and 28 reciting nodes or established position interconnected by established descriptors.

6. The metabolic pathways of organisms are thus modeled using links and nodes, as required by claim 1 and claim 22, step (b) reciting proposing biological model using the representative structure which is the model network, where the plural pairs of nodes are shown by Jeong et al. to be two nodes connected by one link in Figure 1 (a) and (c).

7. Jeong et al. teach simulating the metabolic pathways modeled by a scale-free network to produce data for the diameter of the network with the emergence and deletion of nodes (page 652, col. 2, line 24 to page 653, col. 1, line 7) to find that the diameter of networks representing simple and complex cellular metabolic systems are the same, as required by claim 1 and claim 22, step (c) reciting simulating the proposed biological model to produce simulated data and claims 9 and 30 reciting qualitative simulation techniques used to simulate the proposed model to produce simulated data.

8. Jeong et al. repeat the simulation for 43 different scale-free network models representing the metabolic systems of 43 different organisms (page 652, col. 2, line 24 to page 653, col. 1, line 7; and Figure 3(e)), as required by claim 1 and claim 22, step (e).

9. Jeong et al. teach that their model represents evolution of a biological system as it mimics this with the growth of new nodes that attach to already existing nodes (page 651, col. 1, lines 10-14 from bottom; and page 653, lines 1-4 from bottom) and thus, represents an evolutionary algorithm, as in claims 2 and 23.

10. Jeong et al. teach the modeling of 43 organisms using the scale-free network model, as required by claims 4 and 25 reciting that a biological model comprises a population of biological models. Jeong et al. also teach that the organism data for the modeled cellular networks is based on data taken from the WIT database as required by claims 10 and 31 which recite repeating the method using datasets probing separate biological subsystems. Jeong teaches that each organism is a subsystem of the overall model of cellular activity in the 43 organisms as illustrated in Figure 2(d), and the connectivity distribution is averaged over 43 organisms (page 652). The individual models of the 43 organisms are combined as further required by claims 10 and 31, into a consolidated model because all organisms have an identical metabolic network, according to the model of Jeong et al. (page 653, col. 2, lines 4-4 and 19-22), with uniform network topology observed in all 43 organisms (page 653, col. 2, lines 30-36). Furthermore, each dataset is used to model one of the 43 cellular organisms, as required by claims 11 and 32, wherein the scale-free network model contains disparate

subsystems related to the different substrates produced by different enzymes (Figure 1(e), page 652) wherein these different substrates and enzymes are combined into a consolidated network representing one of the 43 organisms, as required by claims 11 and 32 reciting combining disparate (i.e. different) subsystem networks into a consolidated network.

11. The nodes and links as taught by Jeong et al. in Figures 1 (a), (b) and (e) include substructures or sub-networks which are the interactions between certain enzymes and produced substrate by that enzyme (page 652), as required by claim 15 and 36.

12. Jeong et al. do not teach assigning a fitness measure to the proposed biological model as a measure of how the simulated data compares to data representative of measured biological behavior or properties and selecting one of said proposed biological models in response to the fitness measures of said plurality of biological models, as required in claim 1 and 22, steps (d) and (f). Jeong et al. also do not teach data representative of measured biological behavior to be medical data, as required by claim 19.

13. Park et al. however teach a network data structure for modeling metabolic reactions from data in a database. Park et al. teach models based on a data structure relating a plurality of *Bacillus subtilis* reactants to a plurality of *Bacillus subtilis* reactions [paragraphs 0023, 0024 and 0071]. Park et al. teach that the reactions in a reaction network data structure or metabolic reaction database can be annotated with a value indicating the confidence (i.e. a fitness measure) with which the reaction is believed to occur in B. subtilis. The level of confidence can be a function of the amount and form of

supporting data available such as documented experimental results (i.e. data representative of measured biological behavior) [paragraph 0071]. This reads on the limitation of claim 1, step (d). Furthermore, the in the case of histidine utilization, the simulation model of Park et al showed results contrary to experimental evidence (i.e. another fitness measure) so the model was modified by adding a reaction and it was found that final result of the newly modified model was in agreement with true physiology of the organism (i.e. selecting one of the proposed models) [paragraph 0121], as required by claims 1 and 22, step (f) reciting selecting one of said different proposed biological models in response to the fitness measures of said plurality of biological models.

14. Park et al. further teach that their model can be used to advance research in medicines [paragraph 0024] and identify a drug target and the methods can be particularly useful for identifying a target in a peripheral metabolic pathway [paragraphs 0111-0112]. The candidate drug once identified can be validated using the method of the invention [paragraph 0113], as required by claims 19 and 40 reciting medical (e.g. drug) data and experimental data as the data representative of measured biological behavior. Park et al. also teaches the identification of the drug using experiments after modeling the metabolic pathways [paragraph 0111-0112], as required by claim 21 and 42, which recite conducting biological experiments designed to asses the validity of the biological model.

15. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have implemented the scale-free network model of

cellular metabolisms as taught by Jeong et al. with the method of using a fitness value when comparing modeled data with experimental data and selecting the model based on the fitness value as taught by Park et al. One of skill in the art would have been motivated to use the comparison and choice steps of Park et al. with the method of Jeong because Park et al. teach that their method can be used to guide research and discovery processes, discovery of new enzymes, medicines, or metabolites of commercial importance [paragraph 0023]. One of skill in the art would have had a reasonable expectation of success at utilizing the method of Jeong et al. with the method of Park et al. because both teach modeling metabolic processes of simple unicellular organisms.

16. Claims 8 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jeong et al. in view of Park et al. as applied to claim 1, 2, 4, 7, 9-12, 15, 19, 21-23, 25, 28, 30-33, 36, 40 and 42 above, and further in view of Barabasi et al. (Physica A, vol. 272 (1999) pages 173-187).

17. Jeong et al. in view of Park et al. make obvious a network model where substrates represented by nodes are linked together in biochemical pathways, as set forth above. Jeong et al. in view of Park et al. however do not teach differential equations that quantitatively represent possible relationship between pairs of nodes, as required by claims 8 and 29.

18. Barabasi et al. however teach scale-free networks where the connectivity of individual vertices (i.e. a node) are modeled using differential equations (page 181, lines 1-4 and equation 4; and page 183, lines 1-3 and equation 13).

19. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have implemented the scale-free network model of cellular metabolisms as taught by Jeong et al. in view of Park et al. with the use of differential equations as taught by Barabasi et al. One of skill in the art would have been motivated to use the differential equations as taught by Barabasi et al. because they are able to describe the complex topology common in nature (Barabasi, abstract). One of skill in the art would have had a reasonable expectation of success at utilizing the method of Jeong et al. in view of Park et al. with that of Barabasi et al because both Jeong et al. and Barabsi et al. teach the same scale-free network model comprising links and nodes.

20. Claims 13 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jeong et al. in view of Park et al. as applied to claims 1, 2, 4, 7, 9-12, 15, 19, 21-23, 25, 28, 30-33, 36, 40 and 42 above, and further in view of Jeong et al. (Nature, vol. 411 (2001) pages 41-41)(i.e Jeong 2).

21. Jeong et al. in view of Park et al. make obvious a network model where substrates represented by nodes are linked together biochemical pathways, as set forth above. Jeong et al. in view of Park et al. however do not teach nodes comprising proteins other than enzymes, as required by claims 13 and 34.

22. Jeong 2 however, teach a scale-free network of nodes and links representing the connectivity of protein-protein interactions (page 41 col. 1, 3rd paragraph; and figure 1) wherein each node represents a protein and the links represent the connections between proteins.

23. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have implemented the method of modeling a scale-free network of cellular metabolisms as taught by Jeong et al. in view of Park et al. with the modeling of proteins as nodes as taught by Jeong 2. One of skill in the art would have been motivated to model proteins at taught by Jeong 2 because Jeong 2 teach that proteins are identified as building blocks in cells (Jeong 2, page 41, lines 1-5). One of skill in the art would have had a reasonable expectation of success at utilizing the method of Jeong et al. in view of Park et al. with that of Jeong 2 because both Jeong et al. and Jeong 2 teach using the same scale-free network model comprising links and nodes.

Response to Arguments

4. Applicant's arguments filed 2/12/2008 have been fully considered but they are not persuasive.

5. Applicants argue (Remarks, page 10, ¶ 3-4) that neither Jeong nor Park teach or suggest using a model-level fitness score to determine which model of a population of generated models is most accurate. Applicants further argue that Jeong does not teach assigning a fitness measure to the proposed biological models.

6. In response, the instant claims recite "assigning a fitness measure to the proposed biological model as a measure of how the simulated data compares to data representative of measured biological behavior or properties." This limitation has been interpreted as the assigning of a fitness measure (or score as argued by Applicants) of how well the simulated data compares to measured biological behavior.

7. Joeng et al. in view of Park et al. teach the instant limitation wherein Pack et al. teaches a network data structure for modeling metabolic reactions from data in a database. Park et al. teach models based on a data structure relating a plurality of *Bacillus subtilis* reactants to a plurality of *Bacillus subtilis* reactions [paragraphs 0023, 0024 and 0071]. Park et al. teach that the reactions in a reaction network data structure or metabolic reaction database can be annotated with a value indicating the confidence (i.e. a fitness measure) with which the reaction is believed to occur in B. subtilis. The level of confidence can be a function of the amount and form of supporting data available such as documented experimental results (i.e. data representative of measured biological behavior) [paragraph 0071]. This reads on the limitation of claim 1, step (d) because the confidence as taught by Pack et al. meets the limitation of being a fitness measure (or score) which describes the confidence with which reactions in the network data structure or metabolic reaction database (i.e. proposed biological model) which compare to actual reactions that take place in an actual biological system of B. subtillis as represented by experimental results (i.e. on the measured biological behavior or properties), as recited in the instant claims.

8. Applicants argue (Remarks, page 10-11, connecting ¶) the teachings of Joeng et al. in view of Park et al. do not anticipate or render obvious the calculation of a model fitness score that describes the ability of a model to accurately describe a complex biological function.

9. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., model fitness score that describes the ability of a model to accurately describe a complex biological function) are not recited in the rejected claim(s). Instant claims 1 and 22 currently recite assigning a fitness measure to the proposed biological model as a measure of how data compares to data representing measured biological behavior or properties, which is not equivalent to limitations argued by Applicants.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anna Skibinsky whose telephone number is (571) 272-4373. The examiner can normally be reached on 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lori A. Clow, Ph.D./
Primary Examiner, Art Unit 1631

Anna Skibinsky, PhD

Art Unit 1631